IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Kei Roger Aoki, et al.	Examiner: Anish Gupta
Serial No.: 10/726,904	Group Art Unit: 1654
Filed: December 2, 2003	Confirmation No.: 4172
For: USE OF THE NEUROTOXIC COMPONENT OF A BOTULINUM TOXIN FOR TREATING A SPASTIC MUSCLE	

Board of Patent Appeals and Interferences
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, Virginia 22313-1450

REQUEST FOR REHEARING

Appellant submits this request for rehearing of the Board's decision of May 21, 2010, under 37 C.F.R. § 41.52 because the Board raised a new ground of rejection, and because the Board misapprehended and overlooked certain matters of fact and law. As explained below in section I, Appellant respectfully requests that the Board grant this rehearing request and remand the application to the Examiner for consideration of the Board's new rejection so that Appellant may have a fair opportunity to react to the thrust of the Board's new rejection. In the alternative, as explained below in section II, Appellant respectfully requests that the Board grant this rehearing request and withdraw or reverse the Board's new rejection based on the current appellate record, which demonstrates that the pending claims on appeal are patentable over the Board's new rejection.

Appellant reserves all rights to further appeal or other review.

ARGUMENT

I. The Board raised a new ground of rejection under 35 U.S.C. § 103(a).

On page 3 of the Board's decision, the Board states that the claims stand rejected as follows:

> Claims 1, 2, 4, 5, 29, 47, and 63 under 35 U.S.C. § 103(a) as unpatentable over Balkin or Han in view of Kohl, Tse, and Aoki '915.
>
> Claims 1, 2, 4, 5, 29, 47, and 63 under 35 U.S.C. § 103(a) as unpatentable over Balkin or Han in view of Kohl, Aoki '915, and Aoki '415.

After concluding that Han, Kohl, Aoki '915, and Aoki '415 are not prior art, the Board nevertheless "affirmed" a rejection based on obviousness. In particular, the Board "affirmed" the rejection of claims 1, 2, 4, 5, 29, 47, and 63 under 35 U.S.C. § 103(a) as unpatentable over Balkin and Tse. As explained below, this Board rejection constitutes a new ground of rejection under 37 C.F.R. § 41.50(b). Accordingly, should the Board on rehearing decide not to reverse this Board rejection based on the current appellate record as discussed in section II below, then Appellant respectfully requests that the application be remanded to the Examiner for further consideration of the Board's new rejection so that Appellant may have a fair opportunity to react to the thrust of the Board's new rejection by, for example, submitting an appropriate amendment of the claims and/or a showing of additional facts and evidence.

As explained in *In re Kronig*, 539 F.2d 1300 (C.C.P.A. 1976), the "ultimate criterion of whether a rejection is considered 'new' in a decision by the board is whether appellants have had a fair opportunity to react to the thrust of the rejection." This also is explained in *In re Ansel*, 852 F.2d 1294 (Fed. Cir. 1988), where the court stated that:

> [t]he test for determining whether the board's rejection is 'new' centers on whether the 'basic thrusts' of the board's rejection and the examiner's rejection are different. If the basic thrusts of the two rejections are not the same, then the applicants would not already have had a 'fair opportunity' to respond to the thrust of the board's rejection before the examiner, and the board's rejection can fairly be said to warrant a further opportunity for response.

Denial of this opportunity to respond to a new rejection represents "a deprivation of the applicants' administrative due process rights." *Id.* Appellant notes that the Board in a recent decision states that "[r]eliance upon fewer references in affirming a rejection under 35 U.S.C. § 103(a) does not *normally* constitute a new ground of rejection." *Ex parte Payton*, Appeal No. 2009-004092, Bd. Pat. App. & Inter. (April 29, 2010) (emphasis added). In the instant case, however, the basic thrusts of the Board's rejection and the Examiner's rejection are different such that Appellant has not had a fair opportunity to respond to the thrust of the Board's rejection, and thus the Board's "affirmed" rejection constitutes a new ground of rejection.

The basic thrust of the Examiner's rejection is that Balkin teaches the treatment of strabismus in humans using complexed botulinum toxin type A while the combination of Kohl, Tse, and Aoki '915 allegedly suggests, with the legally required reasonable expectation of success, that a person having ordinary skill in the art would substitute the purified neurotoxic component of a botulinum toxin for the complexed botulinum toxin of Balkin. Clearly, any rebuttal of this rejection directed, for example, toward the reasonable expectation of success of the suggested substitution allegedly provided by the combination of Kohl, Tse, and Aoki '915 must address the combination of the Kohl, Tse, and Aoki '915 teachings and not the teachings of any one of these references individually or in isolation. In fact, patent examiners routinely point out the inappropriateness of arguing against multiple references individually in the context of an obviousness rejection, citing MPEP § 2145(IV); *In re Keller*, 642 F.2d 413, 208 USPQ 871

(CCPA 1981); and *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Thus, the only legally appropriate rebuttal directed toward, for example, the reasonable expectation of success inquiry that Appellant had a fair opportunity to present to the Examiner for consideration required an analysis of the combination of Kohl, Tse, and Aoki '915 with Balkin and not simply a combination of Tse with Balkin.

On the other hand, the basic thrust of the Board's rejection, which is quite different from that of the Examiner's rejection, is that Balkin teaches the treatment of strabismus in humans using complexed botulinum toxin type A while Tse alone allegedly suggests, with the legally required reasonable expectation of success, that a person having ordinary skill in the art should substitute the purified neurotoxic component of a botulinum toxin for the complexed botulinum toxin of Balkin. As pointed out above, Appellant has not had a fair opportunity to present an appropriate response directed toward the basic thrust of the Board's rejection for the simple reason that both patent examiners and the courts require an obviousness inquiry to be directed toward the combined teachings of the cited references and not simply the teachings individually or in isolation.

Moreover, unlike other cases such as *Ex parte Payton*, the Examiner in the instant case specifically informed Appellant at an earlier stage of prosecution during an Examiner interview on May 23, 2007, that the pending claims at that time are patentable over the Balkin and Tse combination. In fact, Appellant's summary of that Examiner interview states that:

> the examiner agreed that if enablement of the claimed subject matter is shown, then priority of the claims to the parent application's December 28, 1993 filing date will be granted and the rejection of claims under 35 U.S.C. section 103(a) as being unpatentable over the combinations of: (1) Balkin (1991) or Han (2001) in view of Tse (1982) and Aoki (U.S. patent 6,113,915 filed in 1999), and; (2) Balkin (1991) or Han (2001) in view of Aoki (U.S. patent 6,113,915 filed in 1999) and Aoki (2001 018415) will all be withdrawn because all the combinations contain one or more references which will then not be prior art with regard to the claims.

Consequently, there was no reason for Appellant to present any further arguments or evidence directed toward the patentability of the claims over the Balkin and Tse combination as both the Examiner and Appellant were in agreement that the Balkin and Tse combination falls short of rendering the claims obvious. In addition, as indicated above, the presentation of any such arguments or evidence by Appellant would not have been considered appropriate or on point as the Examiner's rejection required consideration of the combined teachings of the Kohl, Tse, and Aoki '915 references with Balkin, and not simply Tse by itself with Balkin. It certainly cannot be said that Appellant had a fair opportunity to respond to the Board's rejection when the Examiner himself specifically informed Appellant that the pending claims are patentable over that specific combination of references (Balkin and Tse). As such, it is clear that the basic thrusts of the Board's rejection and the Examiner's rejection are different and that Appellant has not had a fair opportunity to respond to the Board's new rejection based on Tse by itself with Balkin.

Also unlike other cases such as *Ex parte Payton*, the basic thrusts of the Board's rejection and the Examiner's rejection are fundamentally different in that the Board's rejection based on obviousness requires an analysis of the prior art from the perspective of an ordinary skilled artisan as of December 28, 1993 (Board Decision at p. 10), while the Examiner's rejection required an analysis of the prior art from the perspective of an ordinary skilled artisan as of May 21, 2003 (Ex. Ans. at p. 22). As such, Appellant has not had a fair opportunity to respond to the Board's new rejection based on Tse by itself with Balkin from the perspective of an ordinary skilled artisan as of December 28, 1993. It is only now that both the Examiner and Appellant have an opportunity to follow the ruling of the Board setting the ten year earlier proper priority date for (1) a proper understanding of the prior art available against the pending claims and (2) a

proper understanding of the perspective from which an ordinary skilled artisan is to assess the available prior art.

As explained in detail in the next section, the current appellate record establishes that the Board on rehearing should withdraw the Board's new rejection. In the event that the Board on rehearing decides not to withdraw or reverse the Board's new rejection, then in light of each of the points explained above, Appellant respectfully requests that the Board remand the application to the Examiner for further consideration so that Appellant may have a fair opportunity to respond to the thrust of the Board's new rejection.

II. The Board's rejection should be withdrawn based on the appellate record.

During prosecution, the Examiner specifically informed Appellant that the pending claims at that time are patentable over the Balkin and Tse combination should the claims be entitled to the December 28, 1993, priority date. Interview Summary of June 4, 2007, at page 3. Nevertheless, the Board, after ruling that the claims are entitled to the December 28, 1993, priority date, entered a new ground of rejection stating that Balkin in combination with Tse alone renders the claims obvious. For the following reasons, Appellant respectfully requests rehearing and withdrawal of the Board's rejection based on the current appellate record.

A. The Board misapprehended the pending claims.

On page 8 of the decision, the Board stated that "the claims aren't limited to a 'clinical setting.'" This is not true. Independent claims 1, 5, and 29 recite a method for treating strabismus. In each case, the method requires administering a therapeutically effective amount of the recited neurotoxic component to a patient to thereby treat strabismus. As such, the claimed methods (and all supporting Examples in the specification) are clearly limited to a clinical setting. In fact, it is unclear how one would treat strabismus by administering a

therapeutically effective amount of the recited neurotoxic component to a patient in any setting other than a clinical setting.

Therefore, as the Board misapprehended the scope of the claims, Appellant respectfully requests the Board to consider the proper scope of the claims and its effect on the Board's ultimate decision regarding the patentability of the claims over Balkin in combination with Tse alone.

B. The Board overlooked evidence teaching away from the pending claims.

The following two sentences from page 9 of the Board's decision constitute the entire substantive explanation regarding the Board's determination that the claims are unpatentable over Balkin in combination with Tse alone:

> The Examiner found that Balkin 'teaches the administration of botulinum toxin type A and type F for the treatment of strabismus' (Ans. 9), and that Tse teaches that pure neurotoxin produces paralysis in rat muscles, and inhibits release of acetylcholine at the vertebrate neuromuscular junction, just like the corresponding complexed neurotoxin (*id*). We agree with the Examiner's conclusion that "it would have been obvious to one of ordinary skill [in] the art to use pure neurotoxin for the treatment of strabismus because [Tse teaches that] pure neurotoxin has similar activity in the paralysis of muscles as complexed neurotoxin and has similar activity against spontaneous release of actetylcholine [sic]' (*Id.* at 10).[1]

The three paragraphs that follow this section merely summarize several of Appellant's arguments followed by a discussion about how they are not

[1] The Board's characterization of the Examiner's conclusion is incomplete in that the Examiner's conclusion also was because "botulinum toxin complexes (MW greater than 150 kda) may result in [a] slower rate of diffusion of the botulinum toxin away from a site of intramuscular injection" and because there "would be a reasonable expectation of success because Kohl et al. demonstrates a faster paralytic effect with purified botulinum toxin components in humans." Ex. Ans. at 10.

persuasive.[2] At no point does the Board's decision discuss the fact that the Schantz reference teaches away from the claimed invention. This is despite the fact that both Appellant and Examiner repeatedly established the prior art teachings of the Schantz reference in the appellate record. For example, on page 9 of Appellant's Appeal Brief, Appellant discussed the Schantz reference, which is Evidence Exhibit A of Appellant's Appeal Brief, as follows:

> Schantz states that "[b]ecause of its lability the neurotoxin is not practical for medical applications," and "[m]ost recent information concerning the structure and pharmacology of botulinum toxin had been obtained with purified neurotoxins, but it is unlikely that these will be used in a clinical setting." Schantz, at page 82 and 89, respectively.

In addition, on page 12 of Appellant's Appeal Brief, Appellant clarified the record regarding the Schantz reference stating that:

> Applicants actually stated, in response to a rejection of the claims under 35 U.S.C. § 103(a), that "[a]t the time of the filing of the present application, one of ordinary skill would not consider the teachings of the Tse reference regarding the use of pure botulinum toxin to be relevant to clinical treatment, such as the treatment of strabismus in humans. For example, in 1992, Schantz et al. [ ] clearly stated that pure botulinum toxin is so labile that it would not be used in clinical settings." See, Response of September 26, 2006 at page 9. Applicants did NOT state that one of ordinary skill would not consider using the neurotoxic component. Applicants did NOT state that the specification does not enable one of ordinary skill to use the neurotoxic component. Instead, Applicants argued, in response to an obviousness rejection, that one of ordinary skill would not consider the Tse reference to be relevant to clinical treatment. Finally, Applicants did NOT state that Schantz "is correct." Instead, Applicants argued, in response to an obviousness rejection, that the statements in Schantz teach away from the claimed invention.

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[2] Appellant respectfully disagrees with the Board's characterization that these arguments are not persuasive and respectfully requests reconsideration of their effect in light of the proper claim scope and entire record as explained herein.

Moreover, the Examiner, under the heading entitled, "the state of the prior art" on page 5 of the Examiner's Answer presented the following, which includes a lengthy quotation from Appellant's September 26, 2006, office action response:

> In response to an obviousness rejection Appellants stated on the response dated September 26, 2006 that there was a "General Belief That Pure Botulinum Toxin is Clinically Ineffective." Appellants asserted:
>
> **"[A]t the time of the filing of the present application, one of ordinary skill would not consider the teachings of Tse reference regarding use of purified botulinum toxin to be relevant to clinical treatment, such as the treatment of strabismus in humans.** For example, in 1992, Schantz et al. (hereinafter the "Schantz reference") clearly stated that purified botulinum toxin is so labile that it would not be used in clinical settings[.] Specifically, Schantz et al. states:
>
> > Most recent information concerning the structure and pharmacology of botulinum toxin has been obtained with purified neurotoxins, but it is unlikely that these will be used in clinical settings. The toxin complexes are much more stable than neurotoxin and can be diluted and formulated with retention of toxicity. Pure neurotoxins can be kept for several weeks to months in solution in the cold but are inactivated on dilution, formulation, and drying.
>
> Schantz et al., Microbiological Reviews, Mar 1992, p. 80-99, 89, second column, emphasis added, Exhibit 2. Since it is believed at the time of filing the present application that pure botulinum toxin would not be effective for clinical use, one of ordinary skill would not be impelled to combine the teachings of the Tse reference (use of pure botulinum toxin in non-clinical settings, i.e., rat experiments) with the teachings of the Balkan/Han references (use of complexed botulinum toxin in clinical setting for treating strabismus in humans).
>
> It is important to note that Schantz et al. makes the statement quoted above even though Schantz et al. was fully aware that pure botulinum toxin had been tested in rats. For example, the Schantz reference cited the Tse reference on the second column on page 83, and Sellin et al. (Acut Physiol Scan, 983; 119:127-33, hereinafter "the Sellin reference", Exhibit 3) on page 89, which reported on

> experiments similar to that of the Tse reference, i.e., injection of pure botulinum toxin type B into the lower hind limb of a rat to produce paralysis. Nevertheless, the Schantz reference asserted that the use of pure botulinum toxin would be clinically ineffective on page 89."
> "Also, note that Schantz et al. was published much later (1992) than Tse (1982). Moreover, Schantz was published in the year that was much closer in time to the priority filing date (1993) of the claimed invention. **Accordingly, the disclosure of Schantz et al. is more current than Tse, and is more reflective of the state of the art for when the present application was filed.**"

(emphasis in original)

The fact that these sections fall within a discussion regarding enablement does not change the fact that the appellate record clearly sets forth the teaching away evidence of the Shantz reference and that both the Appellant and the Examiner properly presented the teaching away evidence for consideration on appeal. This is particularly true given additional statements from both the Appellant and the Examiner during appeal. For example, Appellant specifically states on page 13 of Appellant's Appeal Brief that:

> Analogous to the Board's positions in Singh, it is completely consistent for the '996 application to enable one of ordinary skill to practice the claimed methods while the statements put forth by Schantz lead one of ordinary skill away from such methods when considering non-obviousness. Analogous to the statement by the Federal Circuit in Singh, the question of whether Schantz teaches away from the present invention is not the primary question bearing on enablement. Instead, the question of whether Schantz teaches away from the present invention relates primarily to obviousness.

On page 20 of the Examiner's Answer, the Examiner confirms the fact that Appellant cited the Shantz reference to establish a teaching away from the claimed invention. In fact, the Examiner specifically stated that "Appellants argue that Shantz et al. was cited to establish a teaching away from the claimed invention."

The Board's failure to discuss the fact that the Schantz reference teaches away from the claimed invention also is despite the fact that the Board quoted the same specific sections from the Schantz reference that constitute direct evidence of teaching away from the claimed invention that both the Appellant and Examiner quoted. See Findings of Fact #6 (FF6) of the Board's decision. Yet, at no point does the Board's new obviousness rejection discuss FF6 or the fact that the Schantz reference teaches away from the claimed invention.

An obviousness determination is decided as a matter of law based on the general factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966) and reaffirmed in *KSR International, Inc. v. Teleflex, Inc.*, 550 U.S. 398, 406-407 (2007). As explained in *In re Haruna*, 249 F.3d 1327, 1335 (Fed. Cir. 2001), a teaching away in the art is relevant to an obviousness inquiry. See also *In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997) ("A prima facie case of obviousness can be rebutted if the applicant . . . can show 'that the art in any material respect taught away' from the claimed invention." (quoting *In re Malagari*, 499 F.2d 1297, 1303 (CCPA 1974)). In this case, the Board committed legal error by not properly considering the teaching away evidence clearly set forth in the prior art Schantz reference and presented in the appellate record. Therefore, as the Board overlooked specific evidence teaching away from the claimed invention, Appellant respectfully requests the Board to reconsider its new rejection based on the entire record including the evidence of teaching away presented in the prior art Schantz reference.

CONCLUSION

For the above-stated reasons, Appellant respectfully requests rehearing and withdrawal of the Board's rejection under 35 U.S.C. § 103(a). Should the Board on rehearing decide not to withdraw the Board's rejection based on the current appellate record as discussed herein, then Appellant respectfully requests that the application be remanded to the Examiner for further

consideration of the Board's new rejection so that Appellant may have a fair opportunity to react to the thrust of the Board's new rejection by, for example, submitting an appropriate amendment of the claims and/or a showing of additional facts and evidence.

No fee is believed due. Please apply any other charges or credits to Deposit Account No. 01-0885.

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